REMARKS

Claims 1, 4, 8, 10, 13-16, and 18 have been amended, and claims 2 and 7 have been cancelled without prejudice or disclaimer. Claims 1, 3-6, and 8-18 are pending in the instant application. No new matter has been added as a result of the above-described amendments. Support for the amendments to the claims can be found in the specification at, for example, page 4, lines 18-26. The objections and rejections set forth in the Office Action have been overcome by amendment.

1. Objection to the claims

The Office Action contains an objection to claim 16 because the term "of" in the first line of step (iii), which was deleted in the Preliminary Amendment dated July 12, 2007, still appears in the claim in strike-through format. The Action states that the deleted text should be omitted from the claim.

Applicants have amended claim 16 to omit the deleted text. Applicants, therefore, respectfully request that this objection be withdrawn.

2. Rejections of claims 13 and 16 under 35 U.S.C. § 112, first paragraph

The Office Action asserts rejections of claims 13 and 16 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Action asserts that Applicants' amendments to claim 13(vi), to recite "***at least*** 15 minutes at 4° C" (emphasis added), and claim 16(iii), to recite "no less than 10 and no more than 30 days," constitute new matter. The Action states that Applicants should specifically point to the support for these amendments in the disclosure.

Applicants have amended claim 13 to recite that the "suspension is incubated for 15 minutes at 4°C," rendering this ground of rejection moot. Applicants respectfully disagree with the Action's assertion that the phrase "no less than 10 and no more than 30 days" in claim 16 constitutes new matter, and contend that the above phrase is equivalent to the term "10-30 days." However, in order to expedite prosecution of the pending claims to allowance, and in Applicants' view because it will have no substantive effect on the proper scope of the pending claims, Applicants have amended claim 16 to recite that the cells are "incubated for 10-30 days." Applicants, therefore, respectfully

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request that the rejections under 35 U.S.C. § 112 be withdrawn.

3. Rejection of claims 1-6, 8, 11, and 13 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 1-6, 8, 11, and 13 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as their invention.

The Action asserts that claim 1 is incomplete for omitting essential steps, such omission amounting to a gap between the steps.

Applicants have amended claim 1 to recite the method steps of centrifugation, separation, suspension, and immuno-isolation. Support for this amendment can be found in the specification at, for example, page 4, lines 18-26. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

The Action also asserts that claim 8 is unclear for reciting that cellular components are washed out of the mammary secretion in a first step, and then reciting that they are stained with antibodies in a second step.

Applicants have amended claim 8 to recite that the "cellular components are washed out of the mammary secretion and retained." Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

The Action also asserts that claim 13 is unclear for reciting steps directed to the isolation of progenitor cells that were already isolated in step (iv) of claim 12, from which claim 13 depends.

Applicants have amended claim 13 to indicate that the steps recited in claim 13 are elaborations of step (iv) of claim 12. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

4. Rejection of claim 18 under 35 U.S.C. § 102

The Office Action asserts a rejection of claim 18 under 35 U.S.C. § 102(b) as being anticipated by Stingl *et al.*, 2001, *Breast Cancer Res. Treat.* 67: 93-109. The Action states that Stingel *et al.* teach the characterization of three types of human breast primitive epithelial progenitor cells by a combination of flow cytometry and in vitro colony assay procedures, and that the characterized cells include bipotent progenitor cells. The Action contends that absent evidence to

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the contrary, the product described in the Stingel *et al.* reference is the same as the product of claim 18.

Applicants have amended claim 18 to recite "[p]luripotent progenitor cells isolated from human mammary secretion," thereby limiting the progenitor cells to "pluripotent progenitor cells." Applicants contend that Stingl *et al.* does not disclose pluripotent progenitor cells, but rather discloses only cells that are already committed to the epithelial cell line. In support of this contention, Applicants direct the Examiner's attention to the last paragraph of column 1, page 94 of Stingl *et al.*, which specifies that the cells obtained by Stingl *et al.* are (unipotent) progenitors that are able to generate either a luminal or a myoepithelial phenotype or bipotent progenitors able to generate both mammary epithelial cell lineages (luminal and myoepithelial) (*see* lines 11-13 of the introduction of Stingl *et al*). The term "bipotent" itself excludes the possibility that these cells are still pluripotent cells that are not yet organ- or tissue-specific cells. At the most, such cells can be grouped with multipotent cells, which are already committed to a specific organ or tissue, but which – even within this already limited group – are only at the most bipotent as disclosed in Stingl *et al.* Furthermore, the cells obtained in Stingl *et al.* are EpCAM+-cells, which means that the epithelial cell adhesion molecule EpCAM is presented on the cell surface. By contrast, pluripotent progenitor cells are functionally different in that they do not present any tissue- or organ-specific proteins, for they are not committed to any specific organ or tissue yet, but are capable of generating all differentiated cells types within the body (*see* page 1, lines 18-19 of the instant specification). Therefore, Stingl *et al.* did not isolate pluripotent progenitor cells in the breast tissue examined, but unipotent and bipotent cells (as the instant Action acknowledges on page 8, lines 6-7). Furthermore, the cells isolated by Stingl *et al.* are not of secretory origin, let alone isolated from human mammary secretion, as recited in amended claim 18. Thus, Stingl *et al.* does not disclose pluripotent progenitor cells isolated from human mammary secretion, and therefore does not anticipate claim 18. In support of the above contentions, Applicants provide the Declaration of Mark Cregan.

Applicants contend that for the reasons discussed above, Stingl *et al.* does not anticipate claim 18. Withdrawal of this rejection is therefore respectfully solicited.

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5. Rejections of claims 1-17 under 35 U.S.C. § 103(a)

a. Young *et al.* in view of Stingl *et al.*

The Office Action asserts a rejection of claims 1, 2, and 6 under 35 U.S.C. § 103(a), as being unpatentable over Young *et al.*, 1997, *Aus. J. Zool.* 45: 423-33 in view of Stingl *et al.*, 2001, *Breast Cancer Res. Treat.* 67: 93-109. The Action states that Young *et al.* describe the identification of cellular components of colostrum and milk of the tammar wallaby, and that some of the isolated cells closely resemble blast cells and may be primitive stem cells or epithelial in origin. The Action also states that Stingel *et al.* teach the characterization of three types of human breast primitive epithelial progenitor cells by a combination of flow cytometry and in vitro colony assay procedures, and that the characterized cells include bipotent progenitor cells. The Action concludes that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Young *et al.* and Stingl *et al.* to isolate human mammary progenitor cells from human milk, since Young *et al.* noted the presence of primitive epithelial stem cells in milk.

Applicants have amended claim 1 to recite "[a] method for isolating pluripotent progenitor cells having stem cell-like characteristics from a human mammary secretion of a male or female human body." Young *et al.* concerns the isolation of immune cells from the milk of the tammar wallaby. Applicants note first that Young *et al.* does not disclose the isolation of cells from human mammary secretion. Applicants also note that Young *et al.* does not disclose the isolation of pluripotent progenitor cells, but rather discloses the isolation of fully differentiated immune cells. In the Young *et al.* reference, these cells are described as being granulated and resembling blast cells (*see* page 425, second paragraph of Young *et al.*). In addition, the size indicated for these cells (8-16 μm) does not correspond to the size of pluripotent progenitor/stem cells, which are much smaller, as described in the "Inventor's Statement" submitted on August 26, 2008.

Applicants respectfully contend that a person skilled in the art would not have been motivated to combine the teachings of Young *et al.* (*i.e.*, that immune cells can be found in the milk of the tammar wallaby) with the teachings of Stingl *et al.*, which concerns a different species (human instead of tammar wallaby), a different "tissue" source (breast tissue instead of mammary secretion), and a different cell type (*i.e.*, epithelial cells). Furthermore, neither Young *et al.* nor Stingl *et al.* discloses the isolation of pluripotent progenitor cells. Thus, a person skilled in the art having knowledge of the teachings of Young *et al.* would not be motivated in any way to even search for an

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isolation method for pluripotent progenitor cells. In addition, even if a person skilled in the art would have turned to Stingl *et al.*, the teachings of this reference relate to three different epithelial cells types, which are at the most bipotent, and can be isolated from human breast tissue. In support of the above contentions, Applicants provide the Declaration of Mark Cregan.

Applicants contend that for the reasons discussed above, Young *et al.* in view of Stingl *et al.* does not result in a *prima facie* case of obviousness with respect to claims 1, 2, and 6. Withdrawal of this ground of rejection is therefore respectfully solicited.

b. Young *et al.* in view of Stingl *et al.* and further in view of Buehring

The Office Action asserts a rejection of claims 1, 3-5, 8, 2, 15, and 16 under 35 U.S.C. § 103(a), as being unpatentable over Young *et al.* in view of Stingl *et al.* and further in view of Buehring, 1990, *J. Dairy Sci.* 73: 956-63. The Action states that in addition to the disclosure of Young *et al.* and Stingl *et al.* set forth in section 5(a) above, Buehring describes the culturing of mammary epithelial cells from milk by pelleting the cells from milk by centrifugation, decanting the supernatant, and resuspending the cell pellets in buffer, recentrifuging, repelleting, and rinsing the pellet, followed by culture in culture medium containing antibiotics and antifungal fungizone. The Action concludes that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Young *et al.*, Stingl *et al.*, and Buehring to isolate the human mammary progenitor cells of Stingl *et al.* from human milk by centrifuging the milk and discarding the supernatant as recited in the pending claims, since Buehring specifically describes the isolation of cells from whole milk by centrifugation and pelleting.

Applicants respectfully contend that a person skilled in the art would not have been able to derive the claimed invention by combining Young *et al.*, Stingl *et al.*, and Buehring. Buehring discloses that bovine mammary epithelial cells (BMEC) can be recovered from cows' milk and can be grown in culture. As with Young *et al.*, Buehring concerns another species (*i.e.*, cows). In addition, Buehring concerns epithelial cells, rather than pluripotent progenitor cells. Moreover, Buehring teaches that some of the large cells originating in the disclosed method show a low capacity to proliferate, *i.e.*, are terminally differentiated (*see* column 1, page 962 of Buehring). This is another indication that these cells cannot be pluripotent progenitor cells, the latter of which would show a high proliferation capacity. Buehring further discloses at column 2, page 960 that the

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presence of keratin in both small and large cells biochemically confirmed the epithelial nature of the cells, as keratins are unique to epithelial cells of mammalian species. Even though the small cells are said to proliferate up to ten doubling levels at column 1, page 962 (according to the author, an indication that not all viable exfoliated epithelial cells are terminally differentiated, which implies that most of them are terminally differentiated), this is another unambiguous indication that the large, as well as the small cells, found by Buehring are already committed to the epithelium and therefore are already differentiated to epithelial cells, since pluripotent progenitor cells would surely not show any presence of keratin.

Applicants contend that for the reasons discussed above, Young *et al.* in view of Stingl *et al.* and further in view of Buehring does not result in a *prima facie* case of obviousness with respect to claims 1, 3-5, 8, 2, 15, and 16. Withdrawal of this ground of rejection is therefore respectfully solicited.

c. Young *et al.* in view of Stingl *et al.* and Buehring and further in view of Nghiem *et al.*

The Office Action asserts a rejection of claims 1, 7, 9, 10, 13, and 14 under 35 U.S.C. § 103(a), as being unpatentable over Young *et al.* in view of Stingl *et al.* and Buehring and further in view of Nghiem *et al.*, 2002, Methods 28: 25-33. The Action states that Nghiem *et al.* describe the isolation of a cell population using antibody-coated magnetic beads, wherein the antibody is attached to the beads by a nucleic acid linker, the cells are isolated by passing the suspension over a strong magnet, and bound cells are liberated from the magnetic beads by treatment with DNAse. The Action concludes that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Young *et al.*, Stingl *et al.*, Buehring, and Nghiem *et al.* to isolate the human mammary progenitor cells of Stingl *et al.* using the process described by Ngheim *et al.*

Nghiem *et al.* discloses several separation methods using magnetic beads, the antibody being attached to the beads by a nucleic acid linker. However, Nghiem *et al.* does not compensate for the shortcomings of Young *et al.*, Stingl *et al.*, and Buehring discussed in sections 5(a) and 5(b) above (*i.e.*, provide any indication that pluripotent progenitor cells can be found in human milk). Applicants therefore contend that Young *et al.* in view of Stingl *et al.* and Buehring and further in

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view of Nghiem *et al.* does not result in a *prima facie* case of obviousness with respect to claims 1, 7, 9, 10, 13, and 14. Withdrawal of this ground of rejection is therefore respectfully solicited.

d. Young *et al.* in view of Stingl *et al.* and Buehring and further in view of Goldman *et al.*

The Office Action asserts a rejection of claims 1, 11, and 15-17 under 35 U.S.C. § 103(a), as being unpatentable over Young *et al.* in view of Stingl *et al.* and Buehring and further in view of U.S. Patent Application Publication No. 2004/0029269 (Goldman *et al.*). The Action states that Goldman *et al.* describe maintenance and feeder-free culture of human ES cells in Example 2, where prior to FACS sorting, the cells are detached form Matrigel-coated plates. The Action concludes that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Young *et al.*, Stingl *et al.*, Buehring, and Goldman *et al.* to culture human mammary progenitor cells of Stingel *et al.* on Matrigel using the process described by Goldman *et al.*

Applicants respectfully contend that a person skilled in the art would not have been able to derive the claimed invention by combining Young *et al.*, Stingl *et al.*, Buehring, and Goldman *et al.* Goldman *et al.* disclose a method of isolating neuronal progenitor cells, oligodendrocyte progenitor cells, or neural stem cells from a population of embryonic stem cells (according to paragraph [0003] of Goldman *et al.*, neural stem cells are the multipotent progenitors of neurons and glia). By describing the cells as "multipotent," the Goldman *et al.* reference implies that the cells are committed at least to the neural cell compartment, and by specifying "progenitors of neurons and glia," even their bipotency. Applicants contend, therefore, that Goldman *et al.* also fails to describe the isolation of pluripotent progenitor cells, and therefore does not compensate for the shortcomings of Young *et al.*, Stingl *et al.*, and Buehring discussed in sections 5(a) and 5(b) above. Applicants therefore contend that Young *et al.* in view of Stingl *et al.* and Buehring and further in view of Goldman *et al.* does not result in a *prima facie* case of obviousness with respect to claims 1, 11, and 15-17. Withdrawal of this ground of rejection is therefore respectfully solicited.

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CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Sajjadi believes it to be helpful, he is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
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Dated: June 26, 2009

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